

- 3 Reid BJ, Haggitt RC, Rubin CE, Rabinovitch PS. Barrett's esophagus: correlation between flow cytometry and histology in detection of patients at risk for adenocarcinoma. *Gastroenterol* 1987;93:1-11.
- 4 Schutte B, Reynders MMJ, Bosman FT, Blijham GH. Flow cytometric determination of DNA ploidy level in nuclei isolated from paraffin-embedded tissue. *Cytometry* 1985; 6:26-30.
- 5 Ralfkiaer E, Wantzin GLK, Larsen JK, Christensen IJ, Thomsen K: Single DNA measurements in benign cutaneous lymphoid infiltrates and in positive patch tests. *Br J Dermatol* 1985;112:253-62.

### Barium sulphate radio-opacity agent and bacterial adhesion to silicone catheter material

Intravascular cannulae are often impregnated with barium salts to render them radio-opaque. The biocompatibility<sup>1</sup> of silicone based polymers makes them a natural choice in the manufacture of longer term intravascular devices, and silicone cannulae impregnated with barium display a greater affinity for bacteria than do other implanted plastics.<sup>2</sup> As divalent cations have a recognised role in the adhesion of micro-organisms to inanimate surfaces<sup>3,4</sup> it is theoretically possible that cannula material impregnated with barium might be more prone to bacterial colonisation and subsequent infection. We investigated this possibility by comparing bacterial adhesion to a silicone cannula material both with and without barium sulphate impregnation.

Dow Corning silicone rubber, grade RX65, was obtained as central venous and drainage cannulae (HG Wallace Ltd, Colchester, England). It contained either no barium sulphate (RX), 8% barium sulphate evenly distributed throughout the polymer (BaS), or a narrow lengthwise strip of barium sulphate (STR). Lengths representing equal surface areas were used and the cannulae were bisected longitudinally to ensure ease of washing during experiments. Six strains each of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli* and *Pseudomonas aeruginosa* were examined. With the exception of the *E coli* strains, all organisms

had been obtained from infected intravascular cannulae. The bacteria were grown overnight on nutrient agar containing <sup>3</sup>H-glucose and washed three times by centrifugation before use. Each strain was suspended in dulbecco AB buffer and 1 ml was placed in a stoppered container along with one of the cannula materials. The containers were tumbled for one hour at room temperature to allow adhesion to take place. At the end of the experiment loosely adherent bacteria were removed by repeated washing in buffer. All experiments were performed in triplicate. When dry, the pieces of cannula were immersed in scintillation fluid and  $\beta$  emissions were counted. The percentage of counts adherent to cannula material are shown in the table.

Comparison of the variance of adhesion of bacteria (F-test) showed no significant differences in adhesion to the three preparations of the polymer.

The above findings indicate that the presence of barium sulphate does not influence the adhesion of bacteria to silicone polymer and that its use as a radio-opacity agent is unlikely to influence bacterial colonisation of intravascular cannulae.

SP BARRETT

K HOWARD

Microbiology Department,  
Southend Hospital, Westcliff-on-Sea,  
Essex SS0 0RY

### References

- 1 Homsey CA. Biocompatibility in selection of materials for implantation. *J Biomed Mat Res* 1970;4:341-56.
- 2 Barrett SP. Bacterial adhesion to intravenous cannulae: influence of implantation in the rabbit and of enzyme treatments. *Epidemiol Infect* 1988;100:91-100.
- 3 McCourtie J, Douglas J. Relationship of cell surface composition of *Candida albicans* and adherence to acrylic after growth on different carbon sources. *Infect Immun* 1981;32:1234-41.
- 4 Stotzky G. Mechanisms of adhesion to clays, with reference to soil systems. In: Savage DC, Fletcher M, eds. *Bacterial adhesion: mechanisms and physiological significance*. New York: Plenum Press, 1985:195-254.

### Hypothyroidism: an important differential diagnosis for raised serum transaminases?

Raised serum transaminase and lactate dehydrogenase activities are often found in the absence of any overt liver dysfunction. When assessing such abnormalities, it is widely believed that hypothyroidism must be considered as this is known to be associated with increases in several serum enzymes including lactate dehydrogenase (LDH), creatine kinase, aldolase, transaminases, malate dehydrogenase and hydroxybutyrate dehydrogenase.<sup>1,2</sup> This association can be of diagnostic importance as clinicians have, on occasion, wrongly attributed increased activities of "cardiac enzymes" in patients with primary hypothyroidism to ischaemic heart disease.<sup>3,4</sup>

Two cases from Torbay Hospital were brought to our attention (Yates, personal communication) in whom asymptomatic primary hypothyroidism was diagnosed following the further investigation of abnormal enzymes on routine blood testing. Both were men aged 61 and 31, respectively, with normal serum bilirubin concentrations and alkaline phosphatase (ALP) activities. Serum aspartate amino transferase (AST), LDH, thyroxine (T4), and thyroid stimulating hormone (TSH), however, were abnormal as shown below. In case 1 AST was 488 U/l (5-40), LDH 717 U/l (150-450), T4 64 nmol (60-160) and TSH 14 mU/l (up to 8). In case 2 AST was 66 U/l, LDH 1057 U/l, T4 17 nmol and TSH greater than 60 mU/l.

Because of these findings we wondered how often increases in serum lactate dehydrogenase and transaminase activities might be explained by previously unsuspected or developing primary hypothyroidism. To test the hypothesis lactate dehydrogenase and aspartate aminotransferase activities were measured on 940 serum samples received by the laboratory for routine liver function tests. Patients from this population were screened for evidence of hypothyroidism if their serum enzyme activities were increased in the absence of overt liver dysfunction—that is, the following criteria were fulfilled:

(i) bilirubin of less than 21 mol/l (normal range 2-20 mol/l); (ii) ALP of less than 150 IU/l (normal range 20-110 IU/l); (iii) LDH greater or equal to 300 IU/l (normal range 0-300 IU/l) or AST greater or equal to 40 IU/l (normal range 0-40 IU/l). Patients from the paediatric and renal departments were excluded.

One hundred and twenty five samples from 62 women and 63 men fulfilled the defined criteria. LDH activities alone were

Table Mean (SD) percentage of inoculated organisms adherent for 18 replicates

Substrate	<i>S epidermidis</i>	<i>S aureus</i>	<i>E coli</i>	<i>P aeruginosa</i>
Silicone (BaS)	16.7 (12.0)	22.6 (25.0)	4.0 (2.7)	50.8 (24.0)
Silicone (STR)	13.5 (11.3)	25.1 (23.5)	4.5 (2.2)	46.9 (24.0)
Silicone (RX)	21.2 (12.0)	36.0 (29.0)	5.2 (3.4)	50.4 (29.0)

Table Identification of patients with overt and borderline hypothyroidism

Case No	Age	Sex	T4 (nmol/l)	TSH (mU/l)	AST (IU/l)	LDH (IU/l)
<b>Hypothyroidism (n = 2):</b>						
1	81	F	64	35.5	29	337
2	67	F	34	50+	33	428
<b>Borderline hypothyroidism (n = 3):</b> (T4 80 - 110 nmol/l; TSH greater than 6.5 mU/l)						
			(a)	(b)	(a)	(a)
1	69	F	81	83	7.1	2.3
2	68	M	103	103	8.3	4.6
3	83	M	82	103	7.5	5.6

(a) = initial blood test results; (b) = repeat blood test result taken three to nine months later.

increased in 92 cases, AST activities alone were raised in 18, and in 16 both enzymes were high. Thyroid function testing consisted of initial duplicate analyses of serum T4 concentrations by radioimmunoassay using donkey anti-sheep antibodies (RAST Allergy Unit, Benenden Chest Hospital) and <sup>125</sup>I (Amersham International) as a tracer. Eighty one of 125 samples with T4 concentrations of less than 110 nmol/l

(normal range 50-160) were then assayed for TSH (Serono Kit). Five of 125 patients (table) were found to have abnormal thyroid function tests. The two cases of frank primary hypothyroidism identified had been diagnosed by the admitting physicians and received treatment before the study results were available. All three borderline cases were asymptomatic for thyroid disease and on follow up showed no progression.

The likelihood that unexpected increases in serum enzymes can be explained by undiagnosed hypothyroidism is minimal and hypothyroidism should therefore be low on the list of differential diagnoses.

EA CLARKE

P YATES

DJ GOLDIE

Department of Pathology,  
Southmead Hospital,  
Bristol BS10 5NB

## References

- 1 O'Malley GR, Davies TJ, Rosenthal FD. Effects of rest exercise and warming on serum creatine kinase levels in primary hypothyroidism. *Clin Sci* 1981;60:595-7.
- 2 Doran GR, Wilkinson JH. The origin of the elevated activities of creatine kinase and other enzymes in the sera of patients with myxoedema. *Clin Chim Acta* 1975;62:203-11.
- 3 White GH, Walmseley RN. Plasma enzyme activities in primary hypothyroidism. *Clin Chem* 1984;30:323-5.
- 4 Huisman JW. Enzyme activities and hypothyroidism. *Clin Chem* 1984;30:1422.

## Matters arising

Bolton General Hospital,  
Minerva Road, Farnworth,  
Bolton BL4 0JR

## Use of necropsy in clinical audit

The views of Hunt on the necropsy in audit are somewhat surprising.<sup>1</sup> Discrepancies between clinical and necropsy diagnoses have been found in several studies,<sup>2,4</sup> and the discrepancies have been regarded as important by clinicians. These findings must not be ignored on the basis of an unjustified comparison with surgical operations. The rather confusing sentence, "It has never been claimed that in hospital medicine more than a few erroneous diagnoses could have been made correctly except by luck" is simply not true. This sentence seems to mean that hospital diagnosis is as good as it possibly can be and cannot be improved. There is a considerable body of evidence to suggest that this is not the case.<sup>5</sup>

No comments are made about quality of necropsy and the need for audit of necropsies. There is considerable disquiet about the quality of some coroners' necropsies on cot deaths, and the number done in a single morning by some pathologists suggests that the quality may not be high. Furthermore, not all coroners' necropsies are performed by properly trained histopathologists. The views expressed by Dr Hunt seem remarkably complacent.

D L BISSET

Department of Histopathology,

## References

- 1 Hunt AC. The necropsy in audit in clinical medicine and other medical specialties. *J Clin Pathol* 1989;42:564-5.
- 2 McGoogan E. The autopsy and clinical diagnosis. *J Roy Coll Phys* 1984;240-3.
- 3 Goldman L, Sayson R, Robbins S, Mettman M, Weisberg M. The value of the autopsy in three medical eras. *N Engl J Med* 1983;308:1000-5.
- 4 Karwinski B, Hartveit F. Death certification: increased clinical confidence in diagnosis and lack of confirmation by necropsy is not justified. *J Clin Pathol* 1989;42:13-17.
- 5 Dowie J, Elstein A. *Professional judgement*. Cambridge: Cambridge University Press, 1988.

## Dr Hunt comments:

It is difficult to reduce a half hour presentation to 500 words, and it is a shame that Dr Bissett did not come to the meeting. I stick by my opinion that most misdiagnoses in modern hospitals follow careful consideration by a medical team and are seldom the result of negligence or lack of individual skill. I dread a return to my early days in pathology when we often were regarded as busybody corpse-cutters trying to teach clinicians their job and were not part of clinical pathology. It is up to clinicians to

regulate their own specialty; it is up to us to provide a high quality necropsy service, which with present staffing levels would be impossible if there were to be a dramatic increase in necropsy numbers, the necessity for which I question. Professor Scheuer recently quoted to me Professor Hamperl's autobiographical account (not available to us monoglots) of the old tradition, "We tried to stop the surgeons sending specimens to us—it was interfering with the real work of the department". And that was in my own lifetime.

The standard of necropsy was not mentioned in my presentation because it was not part of my brief. I share Dr Bissett's disquiet, especially in view of my belief that coroners' necropsies are a particularly important form of audit.

## Clinical importance of squamous metaplasia in invasive transitional cell carcinoma of the bladder

Merely to set the record straight, Martin and colleagues state that with respect to squamous metaplasia an invasive transitional cell carcinoma of the bladder, "Its importance for prognosis is not known," and, "It is only relatively recently that histopathologists have recognised that transitional cell carcinoma with squamous areas is an entity distinct from squamous cell